CHANGES IN CEREBRAL CIRCULATION INDUCED BY HYPNOTIZATION OF THE RABBIT BY THE IMMOBILIZATION METHOD

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16. Abstract Fifteen chinchilla rabbits were hypnotized by fixing them in position on the stomach for 1 min. Electrodes for recording electroplethysmograms and EEG and for polarographic determination of oxygen pressure, and MT-54 thermistors were previously inserted stereotaxically into the sensorimotor cerebral cortex, the dorsal hippocampus, and the reticular formations of the tectum and pons. Arterial pressure was recorded through a catheter inserted into the femoral artery. It was demonstrated that the state of catalepsy in rabbits is accompanied by a sharp enhancement in brain vessel tonus and a decrease in blood flow to all structures investigated. Decrease in brain vessel tone during hypnosis induces the animal to wake up, while an enhanced tone leads to prolongation of hypnosis. The question of possible participation of changes in blood supply to the structures indicated in genesis of hypnosis in immobilized animals is discussed.

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CHANGES IN CEREBRAL CIRCULATION INDUCED BY HYPNOTIZATION OF THE RABBIT BY THE IMMOBILIZATION METHOD

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Much work has appeared in recent years, describing behavioral phenomena and neurophysiological mechanisms of catalepsy (animal hypnosis), induced in animals by forced immobilization of them [13, 16, 22, 25, 26]. Together with neurophysiological changes in animal hypnosis, a number of authors have observed hemodynamic shifts in the central and brain circulation systems [10, 18, 22]. However, the role of the "vascular component" in the genesis of catalepsy has remained unclear up to this time, although there have been individual efforts at theoretical analysis [31]. /1006*

By using electrical stimulation and brain lesions, the special role of the brain stem structure has been successfully revealed [16, 17, 27], and the participation of the neopallium [23, 30] and hippocampus [4] in the genesis of catalepsy has been precisely defined. In connection with this, it seems quite important to study the dynamics of blood supply of the brain structures indicated and to reveal a possible role of circulatory changes in genesis of the phenomenon discussed. Study of this problem was the purpose of this work.

Method

The work was carried out on 15 chinchilla rabbits, weighing 2.5-3.0 kg. Seventy days before the tests, with the animals under

* Numbers in the margin indicate pagination in the foreign text.

nembutal anesthesia, steel, platinum and gold electrodes and MT-54 thermistors were inserted stereotaxically into the sensorimotor region of the cortex, hippocampus, reticular formation of the tegmentum and pons. Recording of the blood flow in each of the structures indicated was accomplished electroplethysmographically (EPG), with two platinum electrodes, 150 μm in diameter, insulated over the entire length, with the exception of the working portion (1.5 mm), and thermoelectrically by means of the thermistors. In the latter case, the state of blood supply to the region studied was determined by change in temperature, considering that the temperature of the brains of rabbits is considerably lower than the temperature of the inflowing blood [2]. The oxygen pressure was recorded with the gold electrodes, and EEG recordings were made on a Nihon Kokden electroencephalograph, with bipolar steel electrodes having a tip diameter of about 30 μm. Systemic arterial pressure was recorded through a catheter inserted into the femoral artery [5].

The tests were conducted on each rabbit over a period of 4-5 days, after which the animals were killed and their brains were examined morphologically. A rabbit was hypnotized by fixing it on the stomach for a period of 1 min. In a portion of the tests, the effect of amyl nitrite and carbon dioxide gas, as well as intravenous administration of papaverine (2 mg/kg) and adrenalin (50 μg/kg), was studied.

Results of Investigation /1007

It is advisable to examine hemodynamic shifts in the brain structures studied during animal hypnosis, on the basis of changes in local temperatures, shifts in the electroplethysmogram levels and the dynamics of its pulsed oscillations.

Local changes in brain temperature, recorded by the thermistor, are unidirectional shifts in all the structures

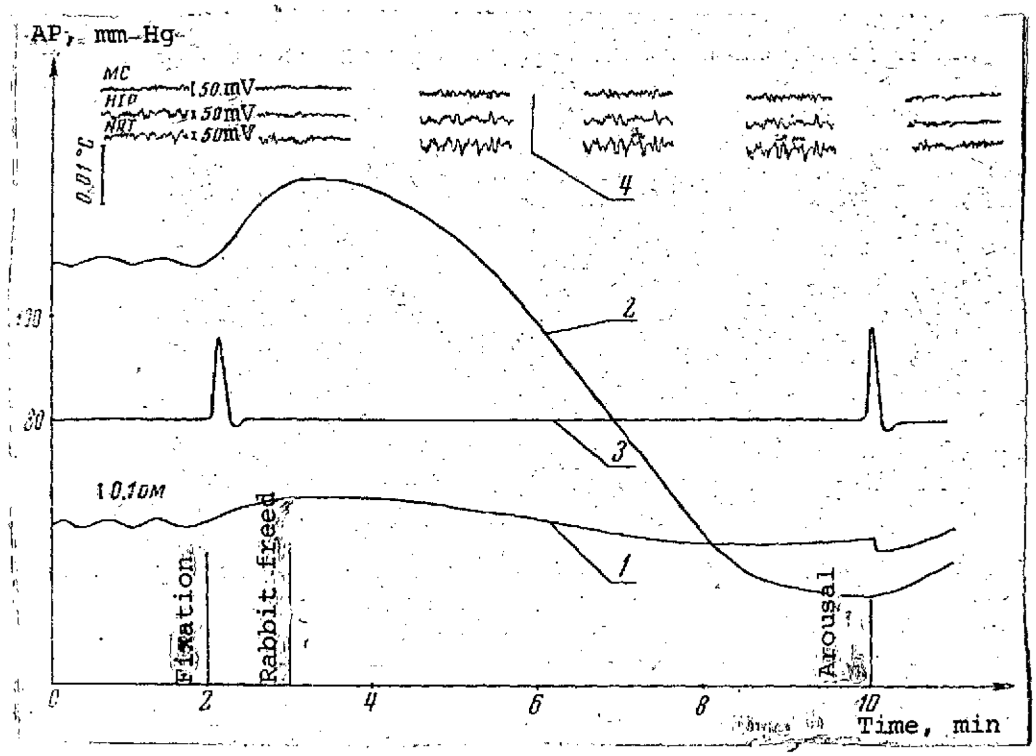

Fig. 1. Diagram of change in constant EPG components (1), brain temperature (2), femoral artery pressure (3) during hypnosis of a rabbit. The data are averaged for four rabbits by structure: sensorimotor cortex, dorsal hippocampus, reticular formations of the tegmentum and reticular formations of the pons. Above, EEG fragments, recorded in control experiment (4).

investigated: in the sensorimotor cortex, in the hippocampus, in the tegmentum of the midbrain and in the reticular nuclei of the pons, the temperature rose during fixation of the animal, reaching a maximum at the moment of stopping fixation. During the hypnosis period, the temperature dropped considerably below the initial level, right up to the start of arousal (maximum shift was 0.015°C). After arousal, the temperature increased sharply to the initial level (Fig. 1).

Local changes in blood flow, estimated from the EPG level, had the same dynamics as the thermograms, disclosing an increase in blood flow during fixation, subsequent decrease in hypnosis, stabilization before arousal and rise after coming out of hypnosis; in this case, the maxima of both curves coincided in time (Fig. 1). It should also be noted that slow temperature fluctuations and the EPG of the brain structures investigated usually appearing distinctly during stimulation, disappeared as a rule during hypnosis, on a background of decreases in these characteristics, and they appeared again after arousal.

The oxygen pressure level did not change noticeably at all at the moment of transition from stimulation to fixation, and only the slow fluctuations observed on the P_{O_2} curve in the background disappeared [5]. During hypnosis, this level remained stable, dis- /1008
playing a tendency to drop before arousal for 40-60 sec, and continued to drop after arousal.

The dynamics of change in the pulsed EPG oscillations were characterized by significant, but negligible (up to 15%) increase in pulse amplitude during fixation of the rabbit, by subsequent decrease of pulse oscillations during hypnosis (by 10-15%), with respect to the background, and by recovery to the background pulse amplitude during arousal. Exceptions were changes in the reticular nuclei of the pons, where a decrease in pulses began at the moment of fixation, with its subsequent decrease with respect to the background by 3-5 times and an increase during arousal, when the level of the pulsed oscillations exceeded the background level by 10-15% (Fig. 2).

Changes in the hemodynamic indicators in the brain during hypnosis were local in nature and were completely independent of systemic factors, in particular, of changes in arterial pressure. The latter did not change during hypnosis. An increase in pressure by 15-20% of the initial level was recorded only during fixation and at the moment of arousal (Fig. 1). The transition processes from stimulation to hypnosis and from hypnosis to stimulation took

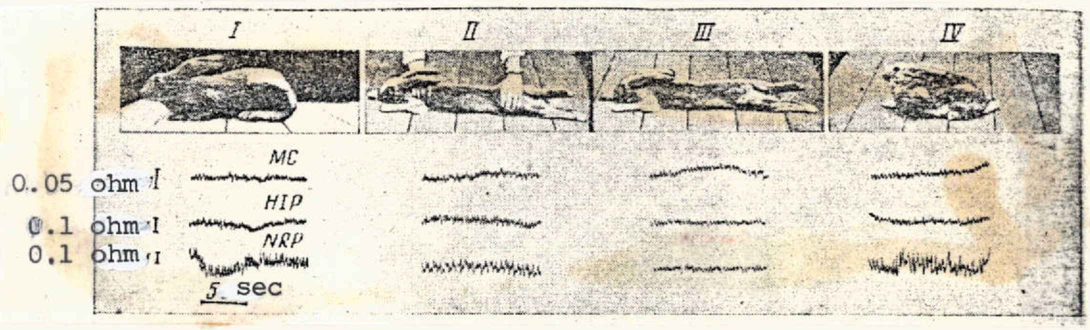

Fig. 2. Changes in pulse EPG oscillations of sensorimotor cortex (MC), dorsal hippocampus (HIP), and reticular nuclei of the pons (NRP) in transition from stimulation (I) to fixation (II), in hypnosis (III) and during arousal (IV).

10-15 sec on the arterial pressure recording and was a consequence of motor activity of the animals.

In this manner, all changes noted in the indices of local brain blood circulation were evidence of a significant reduction in the brain blood flow during hypnosis. This reduction was dependent on an increase in vascular resistance, since the drop in the thermogram and EPG levels, as well as the decrease in pulsed EPG oscillations, on a background of unchanged systolic and diastolic pressure, can only characterize an increase in tonus of the intracerebral vessels.

To pinpoint the role of hemodynamic changes in the genesis of the phenomenon being investigated, a rabbit under hypnosis was presented with substances reducing the tonus of the brain vessels, carbon dioxide, amyl nitrite and papaverine (2 mg/kg intravenously). Five-seven sec after inhalation of the gases or administration of papaverine, the rabbit awoke, on a background of changes characteristic of spontaneous arousal: increase in EPG pulse level, especially in the reticular nuclei of the pons, and increase in temperature of the brain structures investigated, in which these shifts could take place on a background of unchanged arterial pressure.

Studies conducted on nine rabbits, with intravenous administration of adrenalin (50 µg/kg) during hypnosis, demonstrated a significant prolongation of catalepsy, in comparison with the control, to which physiological solution was administered, from 10 to 100% ($P < 0.001$). More than that, in three rabbits not falling under hypnosis after the usual fixation for a period of 1 min, hypnosis could be obtained successfully only after administration of the adrenalin dose indicated during the fixation period. /1009 Twenty-thirty sec after finishing administration of adrenalin, fixation could be stopped: the rabbit was in a state of catalepsy.

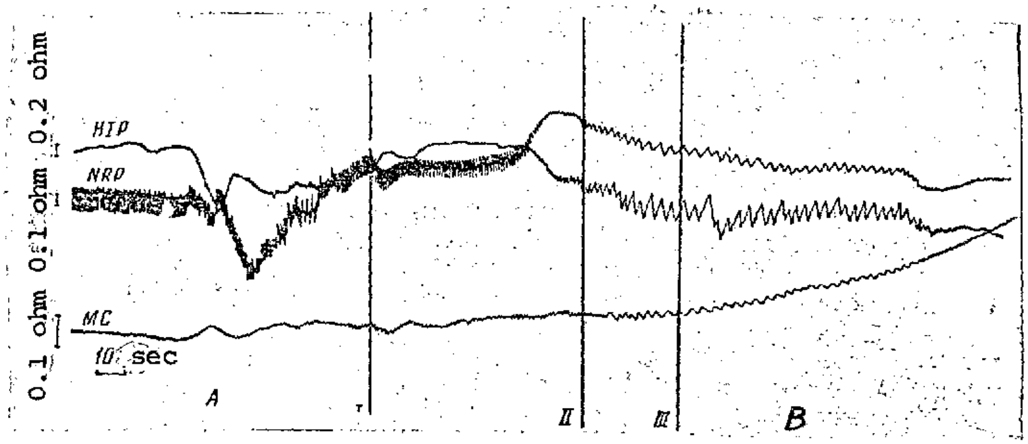

Fig. 3. EPG changes in sensorimotor cortex (MC), dorsal hippocampus (HIP) and reticular nuclei of the pons (RNP) in rabbit during unsuccessful fixation (A) and "putting it to sleep" after intravenous adrenalin administration (I-II), III -- fixation ended, B -- hypnosis.

EPG changes upon administration of adrenalin to rabbits, which "went to sleep" only from this action, deserve attention (Fig. 3): A decrease in EPG pulses in the reticular nuclei of the pons, negligible increase in pulses in the sensorimotor cortex and significant (10-fold) increase in EPG pulses in the dorsal hippocampus. The pulses practically disappeared in all structures after termination of the bradycardia stage and appeared again only upon arousal of the rabbit.

Discussion of Results

The sequence of neurophysiological shifts during hypnosis of a rabbit by the immobilization method has been described previously [13, 16, 27]. The hemodynamic shifts which we noted apparently are accompanied by changes in the bioelectric activity of the structures investigated, and, to a certain extent, they confirm the already well-known assumptions of correlation of blood supply and electrical activity of the brain [5, 20].

The emotional stress arising during forced immobilization of the animal in a position unusual for it [14], is accompanied by a general EEG activation (desynchronization in the cortex and synchronization of the 4-7 Hz rhythm in the subcortical structures). Acceleration of the heart beat and respiration are evidence of a general "arousal reaction." A negligible increase in arterial pressure and an increase in blood supplied to the brain is characteristic of this state. However, an increase in blood flow should not be considered to be a consequence of increased perfusion, since the changes in pressure noted were brief. Vasodilation of the brain vessels during the arousal reaction, described in the literature, can be attributed to functioning of the neurohumoral mechanisms, adapting the blood supply level to the functional state of the brain.

The initial moment of catalepsy itself is formation of inhibition of erector reflexes, mainly in the central apparatus [13], at the stem level, by the nuclei of the "hypnotizing system" [27] and the bulbar reticular formations [16]. The state of catalepsy is accompanied by slow EEG activity, a drop in temperature of the /1010 brain structures and decrease in their filling with blood. These hemodynamic changes are caused by a sharp increase in brain vessel tonus, of which disappearance of the slow spontaneous rhythm of the intracerebral vessels also is evidence [8]. The unchanged oxygen pressure level, even on a background of a decreased supply of it, which most likely of all takes place because of decrease in utilization of it, is evidence of deactivation of thebrain during hypnosis.

Restoration of posture and full arousal of the animal apparently takes place in a manner similar to the transition from the slow phase of sleep to the rapid one [7]. This is indicated by both the characteristic changes in EEG of the structures located at the level of the posterior portion of the midbrain and at the level of the pons [10] and by the increase in blood supply to the regions indicated.

Substances which dilate the brain vessels interrupted the state of catalepsy, which is evidence of the important role of the state of the vascular tonus in genesis of the phenomenon discussed.

The prolonging effect of adrenalin on the state of hypnosis in rabbits can scarcely be explained only by the vessel constricting effect of the preparation [3, 9, 11], which also is confirmed by our data (Fig. 3). Nevertheless, administration of adrenalin apparently aggravates changes in the vascular tonus, together with involvement of the "anticipatory deactivation" mechanisms [6, 12, 15, 19].

The fact of increase in blood supply to the dorsal hippocampus by administration of adrenalin to rabbits, "not sleeping" in control tests, is interesting. This indirectly matches data relative to deepening sleep during stimulation of the hippocampus [7] and increasing its functional activity during electronarcosis [1], and it also agrees with the concepts of Klemm [28] and data on difficulties in hypnotizing rabbits after bilateral coagulation of the dorsal hippocampus [4].

In this manner, electrophysiological shifts during hypnosis of rabbits by the immobilization method quite clearly are correlated with the level of blood supply of the corresponding brain structures, in which the connection of these indices is characterized by a very short time delay. This gives a basis for considering the brain hemodynamics changes noted above to be one possible component in the genesis of the hypnotic state in immobilized animals.

Conclusions

1. The state of catalepsy in rabbits is accompanied by a sharp increase in brain vessel tonus and a decrease in local brain blood flow.

2. By decreasing the brain vessel tonus during hypnosis, arousal of the animal takes place, and an increase in tonus leads to prolongation of the hypnotic state.

3. Changes in blood supply to the structures of the brain stem, hippocampus and neopallium can possibly be considered as one of the likely components of genesis of the hypnotic state in immobilized animals.

REFERENCES

1. Anokhin, P. K. and Sudakov, K. V., Dokl. AN SSSR 192, 934 (1970).

2. Arsen'yeva, V. I. and Gramenitskiy, P. M., in the collection Giperbaricheskiye epilepsiya i narkoz, [Hyperbaric Epilepsy and Narcosis], Leningrad, p. 236.

3. Borkovskaya, Yu. A., in the book Voprosy regulyatsii regionarnogo krovoobrashcheniya, [Problems of Regulation of Regional Blood Circulation], Leningrad, "Nauka" Press, 1969, p. 114.

4. Vaynshteyn, I. I., Mikhaylova, N. G., Paykin, D. I., Pigareva, M. L., Preobrazhenskaya, L. A., and Simonov, P. V., II s"ezd Vses. fiziol. O-va. Materialy simpoz., [Materials of Symposium II Congress of All-Union Physiological Society], Vol. 1, Leningrad, 1970, p. 178. /1011

5. Demchenko, I. T., Dinamika mestnogo mozgovogo krovotoka, [Dynamics of Local Brain Blood Flow], candidates dissertation, Leningrad, 1969.

6. Latash, L. P., in the book Adrenalin i noradrenalin, [Adrenalin and Noradrenalin], Moscow, "Nauka" Press, 1964, p. 751.

7. Lishshak, K., Karmosh, G., and Grashtian, Ye., in the collection Struktury i funktsii nervnoy sistemy. Materialy nauk conf., [Structures and Functions of the Nervous System. Materials of a Scientific Conference], Moscow, 1960, p. 41.

8. Moskalenko, Yu. E., Demchenko, I. T., and Kuper, P., Fiziol. Zh. SSSR 55, 809 (1969).

9. Mchedlishvili, G. I., Byul. Eksperim. Biol. i. Med., (5), 10 (1960).

10. Paykin, D. I., in the book Nervnoye napryazheniye i deyatel'nost' serdtsa, [Nerve Stress and HeartActivity], Moscow, "Nauka" Press, 1969, p. 144.

11. Piotrovich, A. S., in the collection Fiziologiya i patologiya kortiko-vistseral'nykh vzaimootnosheniy i funktsional'nykh sistem organizma, [Physiology and Pathology of the Cortico-Visceral Interrelations and Functional Systems of the Body], Vol. 2, Ivanovo, 1965, p. 160.

12. Simonov, P. V., Tri fazy v reaktsiyakh organizma na vozrastayushchiy stimul, [Three Phases in Reactions of the Body to Increasing Stimuli], Moscow, "Nauka" Press, 1962.

13. Simonov, P. V., Zh. Vyssh. Nervn. Deyat. 13, 140 (1963).

14. Simonov, P. V., Vopr. Psikhologii, (4), 75 (1965).

15. Tonkikh, A. V., Materialy I nauchn. knof. posvyashch. probl. fiziol., morf. i kliniki retikulyarnoy formatsii golovnogo mozga, [Materials of I Scientific Conference Devoted to Problems of Physiology, Morphology and Clinical Aspects of Reticular Formations of the Brain], Moscow, 1960, p. 104.

16. Buser, P., Chertok, L., Fontaine, M., and Viola, G., in Hypnosis and Psychosomatic Medicine, L. Jasner (ed.), 1967, p. 54.

17. Carli, G., Arch. Ital. Biol. 107, 219 (1969).

18. Draper, D. C., and Klemm, W. R., Psychol. Rec. 17, 13 (1967).

19. Gellhorn, E., Acta Neuroveget., (20), 490 (1960).

20. Ingvar, D., Saedy-Moulinier, M., Sulg, J. and Hörman, S., Acta Neurol. Scand. Suppl. 14, 179 (1965).

21. Jouvet, M. and Michel, G., J. Physiol. 52, 130 (1960).

22. Liberson, W. T., Smith, R. W., and Stern. A., J. Neuropsychiatr. 3, 28 (1961).

23. McGraw, P. and Klemm, W. R., Communs. Biol. A3(1), 53 (1969).

24. Kanzow, E., in Neurophysiologia des etats de sommeil, [Neurophysiology of Sleep Conditions], Paris, 1965, p. 231.

25. Klemm, W. R., Lab. Anim. Carc. 15, 163 (1965).

26. Klemm, W. R., EEG and Clin. Neurophysiol. 21, 124 (1966).

27. Klemm, W. R., "Sleep and Wakefulness," Dukes Physiology of Domestic Animals, 8th edition, M. J. Swenson (ed.), Ithaca, New York: Cornell University Press, 1967.

28. Klemm, W. R., Animal Hypnosis, an Experimental Model of EEG-Behavioral Dissocations and Inhibitory Functions of the Brain, Texas A & M University Press, 1968.

29. Klemm, W. R., Communs Biol. A2(1), 43 (1969).

30. Svorad, D., Arch. Neurol. and Psychiatry 77, 533 (1957).

31. Völgyesi, F. A., Hypnosis of Man and Animals, 2nd edition, Williams & Wilkins, Baltimore, 1966.